the petition originally filed August 23, 1996, is present in the prior application where it was improperly directed. The petition filed August 23, 1996, includes a copy of the prior application and the statement verifying the copy as a true copy in compliance with 37 CFR 1.60. The petition will be made of record in the present application where it was intended. Under the circumstances, no petition fee will be required for treatment of this petition.

The petition is granted.

The application is being forwarded to the Office of Finance for scheduling a refund of the $130.00 petition fee paid on August 23, 1996.

Thereafter, the application will be returned to Application Processing Division for processing with a filing date of August 15, 1996, as a continuation application under 37 CFR 1.60, not an application under 37 CFR 1.62, using the specification, drawing and declaration filed August 23, 1996.

Sherry D. Brinkley
Petitions Examiner
Office of Petitions
Office of the Deputy Assistant Commissioner
for Patent Policy and Projects
(703) 305-9220

Conferee: J. F. Gonzales

UNITED STATES PATENT & TRADEMARK OFFICE
Washington, D.C. 20231

REQUEST FOR PATENT FEE REFUND APLST-00619 5E

1 Date of Request: 3-27-97 | 2 Serial/Patent # 08/681684

3 Please refund the following fee(s):	4 PAPER NUMBER	5 DATE FILED	6 AMOUNT
Filing			$
Amendment			$
Extension of Time			$
Notice of Appeal/Appeal			$
✓ Petition 08/335480	4	8-27-96	$ 130
Issue			$
Cert of Correction/Terminal Disc.			$
Maintenance			$
Assigment			$
✓ Other			$

7 TOTAL AMOUNT OF REFUND $ 130

8 TO BE REFUNDED BY:
✓ Treasury Check
Credit Deposit A/C #:
9

10 REASON:
Overpayment
Duplicate Payment
✓ No Fee Due (Explanation):
Fee not necessary.

11 REFUND REQUESTED BY:
TYPED/PRINTED NAME: Karen Creasy TITLE: Legal Inst. Exam.
SIGNATURE: Karen Creasy PHONE: 305-8859
OFFICE: DAC for Patents

THIS SPACE RESERVED FOR FINANCE USE ONLY:
APPROVED: Renee Pulliam DATE: 3/28/97

Instructions for completion of this form appear on the back. After completion, attach white and yellow copies to the official file and mail or hand-carry to:

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Office of Finance
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Crystal Park One, Room 802B

DLEV011748

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, DC 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/691,604	08/15/96	BARBERICH T	0701.027D

12M2/0612

PHILIP E HANSEN
HESLIN AND ROTHENBERG
5 COLUMBIA CIRCLE
ALBANY NY 12203

EXAMINER	
HENLEY III,R	

ART UNIT	PAPER NUMBER
1205	

DATE MAILED: 06/12/97

#6

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (REV. 2/95)

Z-Mail Copy

Office Action Summary

Application No.	Applicant(s)
08/691,604	Timothy L. Barberich, et al.
Examiner	**Group Art Unit**
Ray Henley	1205

☐ Responsive to communication(s) filed on _____

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 1 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-12 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 1-12 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, drawn to a method for treating asthma comprising the administration of the (R-) isomer of albuterol in the absence of its (S+) isomer.

II. Claims 9-12, drawn to a pharmaceutical composition comprising the administration of the (R-) isomer of albuterol in the absence of its (S+) isomer.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process for using the product as claimed can be practiced with another, materially different product such as theophylline.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicants are advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Henley whose telephone number is (703) 308-4652.

RAYMOND HENLEY, III
PRIMARY EXAMINER
GROUP 1200

Henley: rjh
June 10, 1997

12x 12C 6P120

0701.027D #7A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Barberich et al.

Serial No.: 08/691,604 Art Unit: Not assigned 1205

Filed: August 15, 1996 Examiner: Not assigned Henley

Title: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-)ALBUTEROL

MAY 29 1997

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, May 7, 1997.

Philip E. Hansen
Agent for Applicant
Reg. No. 32,700

Date of Signature: May 7, 1997

To: Assistant Commissioner for Patents
Box Non-Fee Amendment
Washington, D.C. 20231

Preliminary Amendment Under 37 C.F.R. 1.115

Dear Sir:

Prior to examination, please amend the application as follows:

In the Claims:

Cancel claims 1-12.

Please add the following claims:

13. A method of treating an acute attack of asthma, while reducing side effects associated with the acute administration of racemic albuterol, comprising administering to an individual

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May 7, 1997

A

suffering from an acute attack of asthma a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

14. A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

15. A method according to Claim ~~13 or 14~~ 23, wherein the albuterol comprises at least 90% by weight of the R(-) isomer and not more than 10% by weight of the S(+) isomer.

16. A method according to Claim ~~13 or 14~~ 23, wherein the albuterol comprises at least 99% by weight of the R(-) isomer and 1% or less by weight of the S(+) isomer.

17. A method according to Claim ~~13 or 14~~ 23, wherein the optically pure R(-) albuterol is administered by inhalation.

18. A method according to Claim 17, wherein the optically pure R(-) albuterol is administered in an amount of about 30 µg to about 90 µg.

~~19~~ 6. A method according to Claim ~~13 or 14~~ 25, wherein the optically pure R(-) albuterol is administered orally.

~~20~~ 7. A method according to Claim ~~19~~ 6, wherein the optically pure R(-) albuterol is administered in an amount of about 1 mg to about 8 mg.

~~22~~ 8. A method according to Claim ~~13~~ 6, wherein the optically pure R(-) albuterol is administered as a syrup.

~~22~~ 9. A method according to Claim ~~20~~ 7, wherein the optically pure R(-) albuterol is administered as a syrup.

~~23~~ 1. A method of treating asthma, while reducing side effects associated with the administration of racemic albuterol, comprising administering to an individual suffering from asthma a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

REMARKS

The present application is a continuation of US application, serial number 08/335,480. Claims 1-12 were present in the application as filed. All claims pending in the original application are canceled by amendment above and are replaced by new claims. Claims 13-23 are therefore pending in this continuation application.

The parent application, 08/335,480, issued to US patent 5,547,994 on August 20, 1996. One week before issue, on August 13, 1996, two references were brought to the attention of applicants' undersigned representative. These references had just been provided by a potential licensee and had not been considered in the prosecution of the '480 case. Although applicants believe that the references are merely cumulative to the references already of record, they did not wish the patent to issue without explicit consideration of the additional references. In accordance with the procedures outlined in the MPEP and in accordance with advice received via telephone from the Office of Petitions, applicants immediately filed a Petition to Withdraw from Issue and a request for File Wrapper Continuation of the '480 case, so that the references could be considered. The Petition to Withdraw from Issue and fee were hand carried to the Office of Petitions on August 15, 1996.

On August 21, 1996, applicants' Petition to Withdraw from Issue was dismissed because there was insufficient time to withdraw the patent. It then became necessary to petition to have the instant application converted from a filing under 37 CFR §1.62 to a continuation under 37 CFR §1.60. A decision mailed on February 28, 1997, granted applicants' petition of August 23, 1996 to effect such a conversion. The application now before the examiner is the culmination of this process.

Claims 13-21 above are presented solely to allow the consideration of the two references not previously cited; the wording of these claims is identical to that of the claims in issued patents 5,362,755 (the parent of this case) and 5,547,994

(the grandparent of this case). As mentioned above, applicants believe that the references are merely cumulative to the references already of record.

The first reference, UK patent 1,298,494, discloses that R(-) albuterol is 50 times more potent than S(+) albuterol in antagonizing acetyl choline-induced bronchoconstriction in the guinea pig (page 1, column 2, line 68-74). The second new reference, German Patent 2,128,258, which corresponds to UK patent 1,298,494, but which has a slightly differently worded specification, refers to the "high pharmacological activity in particular of the R(-) isomers" and discloses without further quantification that R(-) albuterol "functions as an antagonist of the increased bronchial resistance which is caused in anesthetized guinea pigs as a consequence of acetyl choline."

Applicants' reference CB [Brittain *et al.* Brit. J. Pharmacol. 48, 144-147 (1973)], which was discussed extensively during prosecution of the '480 application and its parent 08/163,581, disclosed that mean equipotent doses for (-) and (+) albuterol in acetyl choline-induced bronchoconstriction in the guinea pig were 2.93 and 112 respectively. Thus applicants urge that the two new references add nothing to the existing record, and that the claims that were allowed in the '480 application and its parent, 08/163,581, remain allowable.

Since circumstances have compelled applicants to file this continuation, they have taken the opportunity to add a claim in the clearest possible format. The newly presented claim 23 combines the substance of the claims of the parent (now US patent

5,547,994), which relate to acute medication, with the substance of the claims of the grandparent (US patent 5,362,755), which relate to chronic medication, eliminating the division between acute and chronic, but making no other change. Since claim 23 is not of identical scope to any single claim of either issued patent alone, applicants believe it would not present an issue of statutory double patenting and would be allowable with a terminal disclaimer.

Respectfully submitted,

Philip E. Hansen
Agent for Applicants
Reg. No. 32,700

Dated: May 7, 1997

Address for Correspondence:
Philip E. Hansen
Heslin & Rothenberg, P.C.
5 Columbia Circle
Albany, New York 12203
Telephone: (518) 452-5600
Facsimile: (518) 452-5579

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May 7, 1997

Docket No. 0701.027D

Applicant(s): Barberich et al.

Serial No. 08/691,604 Group Art Unit:

Filed: August 15, 1996 Examiner:

Title: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-) ALBUTEROL

#7

Assistant Commissioner for Patents
Washington, D.C. 20231

STATEMENT OF RELEVANCE FOR INFORMATION DISCLOSED BY APPLICANT

Sir:

The following Statement of Relevance is submitted in regard to reference BC on the Form 1449 submitted August 23, 1996.

Document Designation	Relevance
BC	German Patent 2128258 discloses a process for the preparation of the optical enantiomers of albuterol and in particular the R(-) enantiomer in the form of its acetate methanol solvate. The patent states (column 3, line 30-33) "this purity and the high pharmacological activity in particular of the R(-) isomers are especially useful for the inclusion as active ingredient in medicaments." and (column 3, line 60-64) "the R(-) isomer of the compound of formula I functions as an antagonist of the increased bronchial resistance which is caused in anesthetized guinea pigs as a consequence of acetyl choline (Konzett-Rössler preparation)." The patent describes the synthesis of R(-) and S(-) albuterol and the preparation of tablets and aerosols.

A full text copy of the art cited was submitted, together with Form 1449, on August 23, 1996. It is respectfully requested that this art be considered by the Examiner in the above-entitled application and made of record therein.

Respectfully submitted,

May 7, 1997
Date

Philip E. Hansen
Registration No. 32,700

RCE

#8

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Barberich et al.

Serial No.: 08/691,604 Group Art Unit: 1205

Filed: August 15, 1996 Examiner: Henley III, R.

Title: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-) ALBUTEROL

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on July 11, 1997

Philip E. Hansen
Agent for Applicants
Reg. No. 32,700

Date of Signature: July 11, 1997

To: Assistant Commissioner for Patents
Washington, D.C. 20231

Response to Restriction Requirement
Under 37 C.F.R. 1.143

Dear Sir:

This is a response to the action mailed June 12, 1997 which provided a one month period for response; this response is therefore timely filed. The action requires election under 35 U.S.C. §121 between two groups of claims: Group I

claims 1-8 to a method and Group II claims 9-12 drawn to compositions. Applicants' hereby elect the invention relating to methods (the examiner's Group I) without traverse.

On May 7, 1997, applicants submitted a Preliminary Amendment canceling claims 1-12 and replacing those claims with new claims 13-23. All of the replacement claims relate to a method. Therefore, the election of the method claims now results in the election of claims 13-23. Applicants assume that the Preliminary Amendment had not reached the examiner by the time the Restriction Requirement was issued; they include herewith a copy of the Preliminary Amendment filed May 7, 1997.

Respectfully submitted,

Philip E. Hansen
Agent for Applicants
Registration No. 31,789

Dated: July 11, 1997

HESLIN & ROTHENBERG, P.C.
5 Columbia Circle
Albany, New York 12203
Telephone: (518) 452-5600
Facsimile: (518) 452-5579

0701.027D

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Barberich et al.

Serial No.: 08/691,604 Art Unit: Not assigned

Filed: August 15, 1996 Examiner: Not assigned

Title: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-)ALBUTEROL

#6

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, May 7, 1997.

Philip E. Hansen
Agent for Applicant
Reg. No. 32,700

Date of Signature: May 7, 1997

To: Assistant Commissioner for Patents
Box Non-Fee Amendment
Washington, D.C. 20231

Preliminary Amendment Under 37 C.F.R. 1.115

Dear Sir:

Prior to examination, please amend the application as follows:

In the Claims:

Cancel claims 1-12.

Please add the following claims:

13. A method of treating an acute attack of asthma, while reducing side effects associated with the acute administration of racemic albuterol, comprising administering to an individual

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May 7, 1997

suffering from an acute attack of asthma a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

14. A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

15. A method according to Claim 23 ~~13 or 14~~, wherein the albuterol comprises at least 90% by weight of the R(-) isomer and not more than 10% by weight of the S(+) isomer.

16. A method according to Claim 25 ~~13 or 14~~, wherein the albuterol comprises at least 99% by weight of the R(-) isomer and 1% or less by weight of the S(+) isomer.

17. A method according to Claim 23 ~~13 or 14~~, wherein the optically pure R(-) albuterol is administered by inhalation.

18. A method according to Claim 17, wherein the optically pure R(-) albuterol is administered in an amount of about 30 µg to about 90 µg.

19. A method according to Claim ~~13 or 14~~ 23, wherein the optically pure R(-) albuterol is administered orally.

20. A method according to Claim 19, wherein the optically pure R(-) albuterol is administered in an amount of about 1 mg to about 8 mg.

21. A method according to Claim 19, wherein the optically pure R(-) albuterol is administered as a syrup.

22. A method according to Claim 20, wherein the optically pure R(-) albuterol is administered as a syrup.

23. A method of treating asthma, while reducing side effects associated with the administration of racemic albuterol, comprising administering to an individual suffering from asthma a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

REMARKS

The present application is a continuation of US application, serial number 08/335,480. Claims 1-12 were present in the application as filed. All claims pending in the original application are canceled by amendment above and are replaced by new claims. Claims 13-23 are therefore pending in this continuation application.

The parent application, 08/335,480, issued to US patent 5,547,994 on August 20, 1996. One week before issue, on August 13, 1996, two references were brought to the attention of applicants' undersigned representative. These references had just been provided by a potential licensee and had not been considered in the prosecution of the '480 case. Although applicants believe that the references are merely cumulative to the references already of record, they did not wish the patent to issue without explicit consideration of the additional references. In accordance with the procedures outlined in the MPEP and in accordance with advice received via telephone from the Office of Petitions, applicants immediately filed a Petition to Withdraw from Issue and a request for File Wrapper Continuation of the '480 case, so that the references could be considered. The Petition to Withdraw from Issue and fee were hand carried to the Office of Petitions on August 15, 1996.

On August 21, 1996, applicants' Petition to Withdraw from Issue was dismissed because there was insufficient time to withdraw the patent. It then became necessary to petition to have the instant application converted from a filing under 37 CFR §1.62 to a continuation under 37 CFR §1.60. A decision mailed on February 28, 1997, granted applicants' petition of August 23, 1996 to effect such a conversion. The application now before the examiner is the culmination of this process.

Claims 13-21 above are presented solely to allow the consideration of the two references not previously cited; the wording of these claims is identical to that of the claims in issued patents 5,362,755 (the parent of this case) and 5,547,994

(the grandparent of this case). As mentioned above, applicants believe that the references are merely cumulative to the references already of record.

The first reference, UK patent 1,298,494, discloses that R(-) albuterol is 50 times more potent than S(+) albuterol in antagonizing acetyl choline-induced bronchoconstriction in the guinea pig (page 1, column 2, line 68-74). The second new reference, German Patent 2,128,258, which corresponds to UK patent 1,298,494, but which has a slightly differently worded specification, refers to the "high pharmacological activity in particular of the R(-) isomers" and discloses without further quantification that R(-) albuterol "functions as an antagonist of the increased bronchial resistance which is caused in anesthetized guinea pigs as a consequence of acetyl choline."

Applicants' reference CB [Brittain *et al.* Brit. J. Pharmacol. 48, 144-147 (1973)], which was discussed extensively during prosecution of the '480 application and its parent 08/163,581, disclosed that mean equipotent doses for (-) and (+) albuterol in acetyl choline-induced bronchoconstriction in the guinea pig were 2.93 and 112 respectively. Thus applicants urge that the two new references add nothing to the existing record, and that the claims that were allowed in the '480 application and its parent, 08/163,581, remain allowable.

Since circumstances have compelled applicants to file this continuation, they have taken the opportunity to add a claim in the clearest possible format. The newly presented claim 23 combines the substance of the claims of the parent (now US patent

5,547,994), which relate to acute medication, with the substance of the claims of the grandparent (US patent 5,362,755), which relate to chronic medication, eliminating the division between acute and chronic, but making no other change. Since claim 23 is not of identical scope to any single claim of either issued patent alone, applicants believe it would not present an issue of statutory double patenting and would be allowable with a terminal disclaimer.

Respectfully submitted,

Philip E. Hansen
Agent for Applicants
Reg. No. 32,700

Dated: May 7, 1997

Address for Correspondence:
Philip E. Hansen
Heslin & Rothenberg, P.C.
5 Columbia Circle
Albany, New York 12203
Telephone: (518) 452-5600
Facsimile: (518) 452-5579

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, DC 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/691,604	08/15/96	BARBERICH T	0701.027D

PHILIP E HANSEN
HESLIN AND ROTHENBERG
5 COLUMBIA CIRCLE
ALBANY NY 12203

12M2/0825

EXAMINER	
HENLEY III,R	

ART UNIT	PAPER NUMBER
1205	7

DATE MAILED: 08/25/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

(REV. 2/95)

1-File Copy

Office Action Summary

Application No.	Applicant(s)
08/691,604	Timothy L. Barberich, et al.
Examiner	**Group Art Unit**
Ray Henley	1205

Responsive to communication(s) filed on May 12, 1997 and July 14, 1997.

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- [X] Claim(s) 13-23 is/are pending in the application.
- [ ] Of the above, claim(s) _____ is/are withdrawn from consideration.
- [ ] Claim(s) _____ is/are allowed.
- [X] Claim(s) 13-23 is/are rejected.
- [ ] Claim(s) _____ is/are objected to.
- [ ] Claims _____ are subject to restriction or election requirement.

Application Papers

- [ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.
- [ ] The proposed drawing correction, filed on _____ is [ ] approved [ ] disapproved.
- [ ] The specification is objected to by the Examiner.
- [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
  - [ ] All [ ] Some* [ ] None of the CERTIFIED copies of the priority documents have been
    - [ ] received.
    - [ ] received in Application No. (Series Code/Serial Number) _____.
    - [ ] received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - *Certified copies not received: _____
- [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- [X] Notice of References Cited, PTO-892
- [X] Information Disclosure Statement(s), PTO-1449, Paper No(s). 4
- [ ] Interview Summary, PTO-413
- [ ] Notice of Draftsperson's Patent Drawing Review, PTO-948
- [ ] Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

CLAIMS 13-23 ARE PRESENTED FOR EXAMINATION

Applicants' amendment filed May 12, 1997 has been received and entered into the application. Accordingly, claims 1-12 have been canceled and claims 13-23 added.

Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

(A) Claim 13 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 5,547,994. This is a double patenting rejection.

(B) Claim 14 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 5,362,755. This is a double patenting rejection.

Doctrine of Obviousness-type Double Patenting

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(A) Claims 13 and 15-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,547,994. Although the conflicting claims are not identical, they are not patentably distinct from each other because the choice of a particular dosage amount, form and route of administration would have been a matter well within the purview of the skilled artisan.

(B) Claims 14 and 15-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,362,755. Although the conflicting claims are not identical, they are not patentably distinct from each other because the choice of a particular dosage amount, form and route of administration would have been a matter well within the purview of the skilled artisan.

(C.) Claim 23 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,362,755 and claim 1 of U.S. Patent No. 5,547,994. Although the conflicting claims are not identical, they are not patentably

distinct from each other because as acknowledged by applicants at pages 5-6 of their amendment, present claim 23 combines the substance of both of the above patented claims.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Henley whose telephone number is (703) 308-4652.

RAYMOND HENLEY, III
PRIMARY EXAMINER
GROUP 1200

Henley: rjh
August 12, 1997

Notice of References Cited

Application No:	Applicant(s)		
08/691,604	Timothy L. Barberich, et al.		
Examiner		Group Art Unit	Page 1 of 1
Ray Henley		1205	

U.S. PATENT DOCUMENTS

DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS
5,382,755	11/94	Barberich et al.	514	649
5,547,994	8/96	Barberich et al.	514	649

FOREIGN PATENT DOCUMENTS

DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUBCLASS

NON-PATENT DOCUMENTS

DOCUMENT (Including Author, Title, Source, and Pertinent Pages)	DATE

8/12/97

Trademark Office
(Rev. 9-95) Notice of References Cited Part of Paper No. 9

US005362755A

United States Patent [19]

Barberich et al.

[11] Patent Number: 5,362,755

[45] Date of Patent: Nov. 8, 1994

[54] METHOD FOR TREATING ASTHMA USING OPTICALLY PURE (R)-ALBUTEROL

[75] Inventors: Timothy J. Barberich, Concord; James W. Young, Still River, both of Mass.

[73] Assignee: Sepracor, Inc., Marlborough, Mass.

[21] Appl. No.: 163,581

[22] Filed: Dec. 7, 1993

Related U.S. Application Data

[63] Continuation of Ser. No. 896,725, Jun. 9, 1992, abandoned, which is a continuation of Ser. No. 461,262, Jan. 5, 1990, abandoned.

[51] Int. Cl.[5] A61K 31/135

[52] U.S. Cl. 514/649; 514/826

[58] Field of Search 514/649, 826

[56] References Cited

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2255503 7/1992 United Kingdom .

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D. Hartley and D. Middlemiss, *J. Med. Chemistry*, 14(9):895 (1971).

C. K. Buckner and P. Abel, *J. Pharmacol. Exp. Ther.*, 189(3):616–625 (1974).

Tan et al., "Analysis of Salbutamol Enantiomers in Human Urine by Chiral High Performance Liquid Chromatography and Preliminary Studies Related to the Stereoselective Disposition Kinetics in Man", *J. Chromatogr.*, 422, 187–95 (1987).

Chemical Abstracts 89:123259m (1978).

Primary Examiner—Raymond J. Henley, III

Attorney, Agent, or Firm—Hedin & Rotheaberg

[57] ABSTRACT

The optically pure R(−) isomer of albuterol, which is substantially free of the S(+) isomer, is a potent bronchodilator for relieving the symptoms associated with asthma in individuals. A method is disclosed utilizing the optically pure R(−) isomer of albuterol for treating asthma while minimizing the side effects associated with chronic administration of racemic albuterol.

7 Claims, No Drawings

METHOD FOR TREATING ASTHMA USING OPTICALLY PURE (R)-ALBUTEROL

This application is a continuation of application Ser. No. 07/896,725 filed Jun. 9, 1992 now abandoned which is a continuation of copending application Ser. No. 07/461,262 filed on Jan. 5, 1990 now abandoned.

DESCRIPTION

1. Background

Albuterol is a drug belonging to the general class of beta-adrenergic compounds. The prime action of beta-adrenergic drugs is to stimulate adenyl cyclase, the enzyme which catalyzes the formation of cyclic-3',5'-adenosine monophosphate (AMP) from adenosine triphosphate (ATP). The cyclic AMP formed mediates the cellular responses. Albuterol acts selectively on beta-adrenergic receptors to relax smooth muscle tissue, for example, in the bronchial system. Albuterol is most commonly used to treat bronchial spasms associated with asthma and is the active component in well-known commercial bronchodilators such as Proventil and Ventolin.

The form in which albuterol is presently used is a racemic mixture. That is, it is a mixture of optical isomers, called enantiomers. Enantiomers are structurally identical compounds which differ only in that one isomer is a mirror image of the other and the mirror images cannot be superimposed. This phenomenon is known as chirality. Most biological molecules exist as enantiomers and exhibit chirality. Although structurally identical, enantiomers can have profoundly different effects in biological systems: one enantiomer may have a specific biological activity while the other enantiomer has no biological activity at all, or may have an entirely different form of biological activity.

SUMMARY OF THE INVENTION

The present invention relates to a method of treating bronchial disorders, such as asthma, in an individual, by administering to the individual an amount of optically pure R(−) albuterol which is active in bronchial tissue sufficient to reduce bronchial spasms associated with asthma while minimizing side effects associated with albuterol. The method is particularly useful in treating asthma while reducing side effects, such as central nervous system stimulatory effects and cardiac arrythmia. In these applications, it is important to have a composition which is a potent broncho-dilator and which does not exhibit the adverse side effects of many beta-adrenergic drugs. A composition containing the pure R(−) isomer of albuterol is particularly useful for this application because this isomer exhibits these desired characteristics. The present method provides a safe, effective method for treating asthma while reducing undesirable side effects, for example, tremor, nervousness, shakiness, dizziness and increased appetite, and particularly, cardiac arrythmia, typically associated with beta-adrenergic drugs. In children, side effects such as excitement, nervousness and hyperkinesia are reduced when the pure isomer is administered. In addition to the above, at certain levels racemic albuterol can cause teratogenic effects, which are believed to be associated with the S(+) isomer. Administering the pure isomer reduces the teratogenic potential which is associated with the S(+) isomer of albuterol.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relies on the bronchodilation activity of the R(−) enantiomer of albuterol to provide relief from bronchial disorders, while simultaneously reducing undesirable side effects, for example, central nervous system stimulatory effects and cardiac disorders, commonly experienced by albuterol users. In the present method, the optically pure R(−) isomer of albuterol, which is substantially free of the S(+) enantiomer, is administered alone, or in combination with one or more other drug(s) in adjunctive treatment, to an individual in whom asthma relief (e.g., relief from bronchial spasms, shortness of breath) is desired. The optically pure R(−) isomer of albuterol as used herein refers to the levorotatory optically pure isomer of a'[(tert-butylamino) methyl]-4 hydroxy-m-xylene-α, α'-diol, and to any biologically acceptable salt or ester thereof. The terms "optically pure" or "substantially free of the S(+) enantiomer" as used herein means that the composition contains at least 90% by weight of the R(−) isomer of albuterol and 10% by weight or less of the S(+) isomer. Optically pure albuterol is readily obtainable by methods known to those of skill in the art, for example, by synthesis from an optically pure intermediate.

In the present method, the R(−) isomer of albuterol is administered to an individual who has asthma. For example, R(−) albuterol is administered to an individual after onset of asthma to reduce breathing difficulty resulting from asthma. In another embodiment, optically pure R(−) albuterol is administered prophylactically, that is, before the bronchospasm began in an asthma attack, to prevent its occurrence or to reduce the extent to which it occurs.

In the present method, R(−) albuterol can be administered by inhalation, by subcutaneous or other injection, orally, intravenously, topically, parenterally, transdermally, rectally or via an implanted reservoir containing the drug. The form in which the drug will be administered (e.g., inhalant, powder, tablet, capsule, solution, emulsion) will depend on the route by which it is administered. The quantity of the drug to be administered will be determined on an individual basis, and will be based at least in part on consideration of the individual's size, the severity of the symptoms to be treated and the result sought. In general, quantities of optically pure R(−) albuterol sufficient to reduce the symptoms of asthma will be administered. The actual dosage (quantity administered at a time) and the number of administrations per day will depend on the mode of administration, for example, by inhaler, nebulizer or oral administration. About 30 mcg to about 90 mcg of the optically pure R(−) isomer of albuterol given by inhalation one or more times per day will be adequate in most individuals to produce the desired bronchodilation effect. For oral administration, e.g., tablet or syrup, a dose of about 1 mg to about 8 mg two to four times daily is administered to produce the desired effect.

In the method of the present invention, the optically pure R(−) isomer of albuterol can be administered together with one or more other drug(s). For example, an antiasthmatic drug such as theophylline or terbutaline, or an antihistamine or analgesic such as aspirin, acetaminophen or ibuprofen, can be given with or in close temporal proximity to administration of optically pure, R(−) albuterol. The two (or more) drugs (the

optically pure active isomer of albuterol and another drug) can be administered in one composition or as two separate entities. For example, they can be administered in a single capsule, tablet, powder, or liquid, etc. or as individual compounds. The components included in a particular composition, in addition to optically pure albuterol and another drug or drugs, are determined primarily by the manner in which the composition is to be administered. For example, a composition to be administered in inhalant form can include, in addition to the drug(s), a liquid carrier and/or propellent. A composition to be administered in tablet form can include a filler (e.g., lactose), a binder (e.g., carboxymethyl cellulose, gum arabic, gelatin), an adjuvant, a flavoring agent, a coloring agent and a coating material (e.g., wax or a plasticizer). A composition to be administered in liquid form can include the combination of drugs and, optionally, an emulsifying agent, a flavoring agent and/or a coloring agent.

In general, according to the method of the present invention, the optically pure R(−) isomer of albuterol, alone or in combination with another drug(s), is administered to an individual periodically as necessary to reduce symptoms of asthma.

The present composition and method provide an effective treatment for asthma while minimizing the undesirable side effects associated with albuterol use. These side effects include central nervous system effects, such as tremor, nervousness, shakiness, dizziness and increased appetite, and cardiac effects, such as cardiac arrythmia. In children, side effects, such as excitement, nervousness and hyperkinesia, are reduced when the pure isomer is administered. In addition, teratogenic effects associated with albuterol are believed to reside in the S(+) enantiomer. Thus, administering the pure R(−) isomer may reduce the teratogenic potential associated with albuterol.

Equivalents

Those skilled in the art will recognize, or be able to ascertain, using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed in the scope of the following claims.

We claim:

1. A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of an optically pure R(−) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

2. A method of claim 1 wherein the amount of the R(−) isomer of albuterol is greater than approximately 90% by weight of total albuterol.

3. A method of claim 2 wherein the amount of the R(−) isomer of albuterol is greater than 99% by weight of total albuterol.

4. A method of claim 1 comprising administering to the individual by inhalation from approximately 30 mcg to approximately 90 mcg of the R(−) isomer of albuterol per dose.

5. A method of claim 1 comprising orally administering to the individual from approximately 1 mg to approximately 8 mg of the R(−) isomer of albuterol two to four times daily.

6. A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of an optically pure R(−) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects and at least one additional drug selected from the group consisting of bronchodilators, antihistamines and analgesics.

7. A method of claim 6 wherein the analgesic is selected from the group consisting of aspirin, acetaminophen and ibuprofen.

* * * * *

US005362755A

United States Patent [19]

Barberich et al.

[11] Patent Number: 5,362,755

[45] Date of Patent: Nov. 8, 1994

[54] METHOD FOR TREATING ASTHMA USING OPTICALLY PURE (R)-ALBUTEROL

[75] Inventors: Timothy J. Barberich, Concord; James W. Young, Still River, both of Mass.

[73] Assignee: Sepracor, Inc., Marlborough, Mass.

[21] Appl. No.: 163,581

[22] Filed: Dec. 7, 1993

Related U.S. Application Data

[63] Continuation of Ser. No. 818,723, Jan. 9, 1992, abandoned, which is a continuation of Ser. No. 461,262, Jan. 5, 1990, abandoned.

[51] Int. Cl.[5] A61K 31/135

[52] U.S. Cl. 514/649; 514/826

[58] Field of Search 514/649, 826

[56] References Cited

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Chemical Abstracts 89:123259m (1978).

Primary Examiner—Raymond J. Henley, III

Attorney, Agent, or Firm—Heslin & Rothenberg

[57] ABSTRACT

The optically pure R(−) isomer of albuterol, which is substantially free of the S(+) isomer, is a potent bronchodilator for relieving the symptoms associated with asthma in individuals. A method is disclosed utilizing the optically pure R(−) isomer of albuterol for treating asthma while minimizing the side effects associated with chronic administration of racemic albuterol.

7 Claims, No Drawings

METHOD FOR TREATING ASTHMA USING OPTICALLY PURE (R)-ALBUTEROL

This application is a continuation of application Ser. No. 07/896,725 filed Jun. 9, 1992 now abandoned which is a continuation of copending application Ser. No. 07/461,262 filed on Jan. 5, 1990 now abandoned.

DESCRIPTION

1. Background

Albuterol is a drug belonging to the general class of beta-adrenergic compounds. The prime action of beta-adrenergic drugs is to stimulate adenyl cyclase, the enzyme which catalyzes the formation of cyclic-3',5'-adenosine monophosphate (AMP) from adenosine triphosphate (ATP). The cyclic AMP formed mediates the cellular responses. Albuterol acts selectively on beta2-adrenergic receptors to relax smooth muscle tissue, for example, in the bronchial system. Albuterol is most commonly used to treat bronchial spasms associated with asthma and is the active component in well-known commercial bronchodilators such as Proventil and Ventolin.

The form in which albuterol is presently used is a racemic mixture. That is, it is a mixture of optical isomers, called enantiomers. Enantiomers are structurally identical compounds which differ only in that one isomer is a mirror image of the other and the mirror images cannot be superimposed. This phenomenon is known as chirality. Most biological molecules exist as enantiomers and exhibit chirality. Although structurally identical, enantiomers can have profoundly different effects in biological systems: one enantiomer may have a specific biological activity while the other enantiomer has no biological activity at all, or may have an entirely different form of biological activity.

SUMMARY OF THE INVENTION

The present invention relates to a method of treating bronchial disorders, such as asthma, in an individual, by administering to the individual an amount of optically pure R(−) albuterol which is active in bronchial tissue sufficient to reduce bronchial spasms associated with asthma, while minimizing side effects associated with albuterol. The method is particularly useful in treating asthma while reducing side effects, such as central nervous system stimulatory effects and cardiac arrythmia. In these applications, it is important to have a composition which is a potent broncho-dilator and which does not exhibit the adverse side effects of many beta-adrenergic drugs. A composition containing the pure R(−) isomer of albuterol is particularly useful for this application because this isomer exhibits these desired characteristics. The present method provides a safe, effective method for treating asthma while reducing undesirable side effects, for example, tremor, nervousness, shakiness, dizziness and increased appetite, and particularly, cardiac arrythmia, typically associated with beta-adrenergic drugs. In children, side effects such as excitement, nervousness and hyperkinesia are reduced when the pure isomer is administered. In addition to the above, at certain levels racemic albuterol can cause teratogenic effects, which are believed to be associated with the S(+) isomer. Administering the pure isomer reduces the teratogenic potential which is associated with the S(+) isomer of albuterol.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relies on the bronchodilation activity of the R(−) enantiomer of albuterol to provide relief from bronchial disorders, while simultaneously reducing undesirable side effects, for example, central nervous system stimulatory effects and cardiac disorders, commonly experienced by albuterol users. In the present method, the optically pure R(−) isomer of albuterol, which is substantially free of the S(+) enantiomer, is administered alone, or in combination with one or more other drug(s) in adjunctive treatment, to an individual in whom asthma relief (e.g., relief from bronchial spasms, shortness of breath) is desired. The optically pure R(−) isomer of albuterol as used herein refers to the levorotatory optically pure isomer of α¹[(tert-butylamino) methyl]-4-hydroxy-m-xylene-α, α'-diol, and to any biologically acceptable salt or ester thereof. The terms "optically pure" or "substantially free of the S(+) enantiomer" as used herein means that the composition contains at least 90% by weight of the R(−) isomer of albuterol and 10% by weight or less of the S(+) isomer. Optically pure albuterol is readily obtainable by methods known to those of skill in the art, for example, by synthesis from an optically pure intermediate.

In the present method, the R(−) isomer of albuterol is administered to an individual who has asthma. For example, R(−) albuterol is administered to an individual after onset of asthma to reduce breathing difficulty resulting from asthma. In another embodiment, optically pure R(−) albuterol is administered prophylactically, that is, before the bronchiospasm begins in an asthma attack, to prevent its occurrence or to reduce the extent to which it occurs.

In the present method, R(−) albuterol can be administered by inhalation, by subcutaneous or other injection, orally, intravenously, topically, parenterally, transdermally, rectally or via an implanted reservoir containing the drug. The form in which the drug will be administered (e.g., inhalant, powder, tablet, capsule, solution, emulsion) will depend on the route by which it is administered. The quantity of the drug to be administered will be determined on an individual basis and will be based at least in part on consideration of the individual's size, the severity of the symptoms to be treated and the result sought. In general, quantities of optically pure R(−) albuterol sufficient to reduce the symptoms of asthma will be administered. The actual dosage (quantity administered at a time) and the number of administrations per day will depend on the mode of administration, for example, by inhaler, nebulizer or oral administration. About 30 mcg to about 90 mcg of the optically pure R(−) isomer of albuterol given by inhalation one or more times per day will be adequate in most individuals to produce the desired bronchodilation effect. For oral administration, e.g., tablet or syrup, a dose of about 1 mg to about 8 mg two to four times daily is administered to produce the desired effect.

In the method of the present invention, the optically pure R(−) isomer of albuterol can be administered together with one or more other drug(s). For example, an antiasthmatic drug such as theophylline or terbutaline, or an antihistamine or analgesic such as aspirin, acetaminophen or ibuprofen, can be given with or in close temporal proximity to administration of optically pure, R(−) albuterol. The two (or more) drugs (the

optically pure active isomer of albuterol and another drug) can be administered in one composition or as two separate entities. For example, they can be administered in a single capsule, tablet, powder, or liquid, etc. or as individual compounds. The components included in a particular composition, in addition to optically pure albuterol and another drug or drugs, are determined primarily by the manner in which the composition is to be administered. For example, a composition to be administered in inhalent form can include, in addition to the drug(s), a liquid carrier and/or propellent. A composition to be administered in tablet form can include a filler (e.g., lactose), a binder (e.g., carboxymethyl cellulose, gum arabic, gelatin), an adjuvant, a flavoring agent, a coloring agent and a coating material (e.g., wax or a plasticizer). A composition to be administered in liquid form can include the combination of drugs and, optionally, an emulsifying agent, a flavoring agent and/or a coloring agent.

In general, according to the method of the present invention, the optically pure R(−) isomer of albuterol, alone or in combination with another drug(s), is administered to an individual periodically as necessary to reduce symptoms of asthma.

The present composition and method provide an effective treatment for asthma while minimizing the undesirable side effects associated with albuterol use. These side effects include central nervous system effects, such as tremor, nervousness, shakiness, dizziness and increased appetite, and cardiac effects, such as cardiac arrythmia. In children, side effects, such as excitement, nervousness and hyperkinesis, are reduced when the pure isomer is administered. In addition, teratogenic effects associated with albuterol are believed to reside in the S(+) enantiomer. Thus, administering the pure R(−) isomer may reduce the teratogenic potential associated with albuterol.

Equivalents

Those skilled in the art will recognize, or be able to ascertain, using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed in the scope of the following claims.

We claim:

1. A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of an optically pure R(−) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects, said R isomer being substantially free of its S(+) isomer.

2. A method of claim 1 wherein the amount of the R(−) isomer of albuterol is greater than approximately 90% by weight of total albuterol.

3. A method of claim 2 wherein the amount of the R(−) isomer of albuterol is greater than 99% by weight of total albuterol.

4. A method of claim 1 comprising administering to the individual by inhalation from approximately 30 mcg to approximately 90 mcg of the R(−) isomer of albuterol per dose.

5. A method of claim 1 comprising orally administering to the individual from approximately 1 mg to approximately 8 mg of the R(−) isomer of albuterol two to four times daily.

6. A method of treating asthma in an individual with albuterol, while reducing side effects associated with chronic administration of racemic albuterol, comprising chronically administering to the individual a quantity of an optically pure R(−) isomer of albuterol sufficient to result in bronchodilation while simultaneously reducing undesirable side effects and at least one additional drug selected from the group consisting of bronchodilators, antihistamines and analgesics.

7. A method of claim 6 wherein the analgesic is selected from the group consisting of aspirin, acetaminophen and ibuprofen.

* * * * *